Volume 330, number 2, 242 FEBS 12941 September 1993

Commentary Response

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Received 20 July 1993

In this reply, we give some historical background about our involvement in the classification of aminotransferases, and in particular in the definition of a new class now termed Class V aminotransferases (A. Bairoch, pers. communication), and then describe the complementary nature of the work of the two groups. Early in 1992, we undertook the task of analyzing the recently sequenced chromosome III ORFs from yeast [Oliver, S.G. et al., Nature 357, 38–46]. Apart from verifying the initial results, we were able to identify 17 more ORFs with homology to proteins of known function [Bork, P. et al., Nature 358, 287]. The complete work was published with some delay (Bork, P. et al., Protein Sci. 1, 1677–1690]. The identification of a gene with strong similarity to NifS from nitrogen-fixing bacteria came as a surprise (see also Science 256, 730).

We felt that we should investigate the matter further, and our analysis showed that NifS is homologous to various pyridoxal-5′-phosphate-dependent enzymes. This result was obtained in the summer of 1992, and the manuscript was written before the end of that year. When the Mehta and Christen paper appeared early in 1993 [Mehta, P.K. and Christen, P., Eur. J. Biochem. 211, 373–376], we responded immediately as we submitted the final version of our manuscript by citing the observation of Mehta and Christen, as confirming our results. We believe that both papers make a contribution in complementary ways.

On the methodological side, the two publications are complementary to each other. Our method is an iterative profile search as implemented by Gribskov [Gribskov, M., Gene 119, 107–111] with an additional length constraint. A neural network secondary structure prediction based on multiple alignments [Rost, B. and Sander, C., Nature 360, 540] was also carried out, and the predicted structure around the putative cofactor ligand was presented. In addition, we presented a dendrogram from UPGMA clustering of the sequences.

As far as results are concerned, we explicitly showed the relationship between serine-pyruvate aminotransferases and two proteins defined as soluble hydrogenase small (42 kDa) subunits (later also published by de Zoysa, P.A. and Danpure, C.J., Mol. Biol. Evol. 10, 704–706), isopenicillin *N*-epimerase (in Mehta and Christen referred to as an unpublished result), and phosphoserine aminotransferases (previously thought to form an independent family, and not included in the Mehta and Christen paper). Arguments about the possible role of NifS in amino acid interconversion during nitrogen fixation were also given.

In general, we focused on a particular class and delineated evolutionary relationships between its members. Detailed presentation of sequence similarity, cut-off levels for profile searches, and discussions on each family within the class were given. Aspects of possible functional relationships were also presented. All the above items of our paper appeared for the first time in the literature. The Priority Paper by Mehta and Christen contained preliminary information, with extensive references to unpublished results.

Later in 1993, a paper containing much of the unpublished results appeared [Mehta, P.K., Hale, T.I. and Christen, P., Eur. J. Biochem. 214, 549–561]. This interesting additional report shows the remote evolutionary relationships between aminotransferase classes. We acknowledge the authors' contribution to this problem, and we take the opportunity to congratulate them on their work. We agree with Mehta and Christen that identical scientific results may be obtained by two different groups at virtually the same time. In the end, what matters most, in our opinion, is the intrinsic value of a scientific contribution, rather than the strict order in which publications appear.

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